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PANCREATODUODENAL RESECTION*

A Preliminary Report of Eighteen Cases

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DURING the past decade a new field in abdominal surgery has been explored with the successful removal of the duodenum and pancreas for malignant tumors by a radical block pancreatoduodenal resection. Previously, all attempts to remove carcinomas in this area had been confined to local excisions of malignant tumors of the duodenum or ampulla of Vater, which, in the light of the present knowledge, could be considered little more than palliative resections, with a small chance for complete extirpation of the tumor. Furthermore, these excisions were frequently followed by serious complications, such as retroperitoneal sepsis, external and internal fistulas and strictures of the common bile duct and pancreatic duct. The radical removal of tumors at other sites, such as carcinomas of the breast, stomach, colon and rectum and uterus, has been proved conclusively to give the best results. If it can be demonstrated that the block type of resection (pancreatoduodenal resection) for malignant tumors in this region can be feasibly done with few complications and a low operative mortality, it may then be accepted and more widely applied. Experiences at the Lahey Clinic with 18 resections of this type are presented in the hope of furthering interest in these cases, which are usually considered hopeless.

HISTORY

Although Halsted[1] performed a local excision of carcinoma of the ampulla as early as 1898, and Mayo[2] resected a hyperfunctioning carcinoma of the pancreas in 1927, it remained for Whipple,[3] in 1935, to focus interest on these cases when he and his associates reported a successful resection. Since that time Hunt[4] has reported 4 cases, with a review of the literature, including both local and radical operations, Trimble[5] has reported a successful one-stage operation, and Harvey and Oughterson[6] have reported 6 cases, not all of them radical. More recent reports by Brunschwig[7] and Gray[8] and previous reports by me[9–11] indicate a growing interest in the field. Approximately 100 operations that could be termed radical in the usual sense applied to the surgical treatment of malignant tumors have been performed.

GENERAL CONSIDERATIONS

From our experiences with these cases, approximately 30 per cent of malignant tumors causing jaundice as a primary symptom are suitable for resection. One of the most difficult problems in the management of such cases is that of establishing the diagnosis at operation when it has been suspected preoperatively. The clinical course of carcinoma of the pancreas and carcinoma of the ampulla is quite similar. As shown by Kiefer,[12,13] the development of symptoms associated with carcinoma of the pancreas is slow, with jaundice developing somewhat late, with weight loss, anemia and cachexia appearing first. We have found that in patients with carcinoma of the ampulla, jaundice is the presenting symptom, with the general systemic effects following. Unless a palpable mass is present, the time of development of jaundice is the only clinical means of differentiating these two conditions. In the past the diagnosis of carcinoma of the pancreas has been made in all cases of painless jaundice, irrespective of the order of the development of the symptoms. In our experience, carcinoma of the ampulla is more frequent than carcinoma of the pancreas. Since jaundice develops late with cancer of the pancreas, many of these cases are unsuitable for resection, since metastases or local spread makes it impossible. The degree of malignancy is high in cancer of the pancreas and low in cancer of the ampulla, and it is our experience that most carcinomas of the ampulla are suitable for resection.

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There may be considerable difficulty in proving the presence of cancer at the time of operation. Biopsies of the pancreas when taken as deeply as possible from a pancreatic mass obviously cancerous are frequently negative. Tumors of the ampulla are usually small, being 1 to 2 cm. in diameter even three to six months after they have produced obstruction of the common bile duct, and are difficult to palpate through the head of the pancreas or duodenum. The head of the pancreas frequently has extensions and divisions, due to its racemose character, that on palpation may be confused with tumor. We have explored 3 cases at a second stage, in which a tumor was palpated at the first stage, without finding a tumor, and one resection carried out in a fourth patient with a palpable tumor but cancer could not be demonstrated microscopically. It is important to emphasize the difficulties of establishing the diagnosis at operation, and it is necessary in many cases to do the radical operation without the benefit of a positive biopsy. If cancer is shown by biopsy to be present in the gastrohepatic or gastrocolic ligaments, the radical operation may not be justified. A positive diagnosis can be established by transduodenal exploration of the ampulla, since cancerous tissue can readily be procured. Dilatation of the common duct has been present in all our cases in which cancer was proved. The 3 patients who had an exploratory second stage with the possibility of resection did not have dilated common ducts. In cases in which malignancy cannot be proved, unless dilatation of the common duct is present, resection should not be done. It has been our experience in patients with carcinoma of the ampulla that biopsy is unnecessary, since the projecting tumor can usually be palpated through the duodenal wall.

General Operative Plan

Pancreatoduodenal resection is a formidable operative procedure (Fig. 1) that is time-consuming and difficult, and good operating conditions are essential. We prefer fractional spinal anesthesia, using pontocaine weighted with glucose, with 40 to 50 mg. of the drug in divided doses of 15, 10, 10 and 10 mg., since the operation may take two and a half to four and a half hours. Two transfusions are usually given during the procedure.

The major operative problems are the control of the blood supply as it enters the general field by ligating large vessels and the interruption and restoration of continuity of the gastrointestinal tract, the biliary tract and the pancreas. In the earlier reported cases it was considered unnecessary to restore the pancreatic juice to the intestine, and several successful cases were reported in which no external pancreatic fistula developed and no spontaneous internal fistula could be proved, and in which good health was maintained in spite of its loss. It is our opinion, however, that many of the complications following pancreatoduodenal resection are related to internal or external pancreatic fistulas in spite of ligation of the pancreas and its duct.

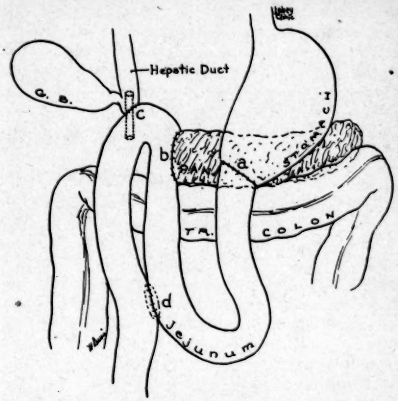

Figure 1. *The Completed One-Stage Pancreatoduodenal Resection.*

All anastomoses are antecolic. a — *end-to-end gastrojejunostomy;* b — *end-to-side pancreatojejunostomy;* c — *end-to-side choledochojejunostomy; and* d — *jejunojejunostomy.* (*Reproduced from Cattell*[11] *with permission of the publisher.*)

This was true in our first case, in which digestion of the stump of the gastroduodenal artery resulted in hemorrhage. Similarly, a longer convalescence may result and retroperitoneal sepsis is likelier to follow. I have previously described a technic of anastomosis of the duct of Wirsung to the jejunum to avoid pancreatic fistula (Fig. 2). The re-establishment of the biliary tract is not difficult, and in the one-stage operation the common duct is anastomosed to the jejunum, whereas in the two-stage operation a cholecystjejunostomy is performed at the first stage. The third or fourth portion of the duodenum has been reported as used for both the pancreatic and biliary anastomoses, but we have utilized a long loop of jejunum for this purpose. It is preferable to use a defunctionalized loop of jejunum, which can be accomplished by side-to-side jejunojejunostomy or by utilizing the Roux principle as described by Whipple.[3] Jejunojejunostomy is unnecessary if the stomach is joined to the efferent jejunum below the pancreatic and biliary anastomoses.

Operation

The first step of operation is to establish the diagnosis by the means outlined earlier in this paper, following which operability is determined. If the patient's condition justifies a one-stage operation, a dissection of the entire field can be carried out with good mobilization without dividing either

the gastrointestinal or the biliary tract. Extension of the tumor makes resection inadvisable. If the superior mesenteric vessels are found to be involved and cannot be freed, this can be determined early in the dissection. If these are freed, the portal vein is then exposed and a finger is placed under the neck of the pancreas to be sure that it can be detached. If the case is deemed inoperable, some benefit may follow ligation of the gastroduodenal artery and inferior pancreatoduodenal artery in continuity. In a patient with complete obstruction of the duct of Wirsung we were able to do a side-to-side anastomosis in continuity between the dilated duct creatoduodenal area should be avoided if possible in this stage. I recommend that a cholecystjejunostomy be done 30 to 45 cm. from the ligament of Treitz, and accompanied by jejunojejunostomy 15 or 20 cm. proximal to the cholecystjejunostomy. The enteroenterostomy defunctionalizes the loop of jejunum used for the biliary anastomosis, and at the second stage the pancreatojejunal anastomosis can be made in the afferent loop distal to the jejunojejunostomy. This biliary anastomosis is simple to perform, and if the omentum is drawn down over it the field for the pancreatoduodenal resection will be uncomplicated by adhesions at the second stage.

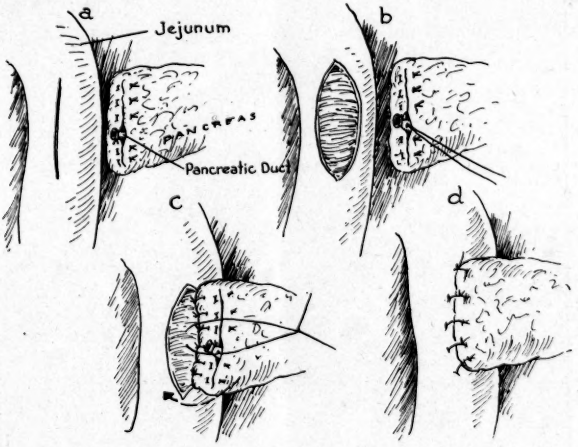

FIGURE 2. *A Technical Method of Avoiding External Pancreatic Fistula.*
a — *the serosal and muscular layers of the jejunum have been incised, the incised pancreas has been closed, and the pancreatic duct has been ligated*; b — *the serosa and muscularis have been spread, and the pancreatic duct has been transfixed by a silk suture*; c — *the posterior surface of the pancreas has been joined to the lateral wall of the jejunum, and the transfixing silk suture now transfixes the mucosa of the jejunum*; and d — *the pancreatojejunal anastomosis is completed by the anterior suture line. (Reproduced from Cattell[9] with permission of the publisher.)*

and the jejunum, with considerable temporary improvement in the patient's condition.

There is as yet no unanimity of opinion relative to the employment of the one-stage versus the two-stage operation for these cases. In my opinion, the two-stage operation should be employed if jaundice is severe, with the bilirubin over 5 mg. per 100 cc., if the liver function is shown to be low by liver-function tests or if the patient's general condition is poor. Since jaundice is usually the presenting symptom, many of these cases can be done in two stages with less risk. If the two-stage operation is chosen, the first stage should consist solely of an anastomosis of the biliary tract to the intestine. Any exploration of the common duct or of the pancreatoduodenal area should be avoided if possible in this stage. There is little question that the patient will be much improved after the first stage and that a definite lowering of operative risk will result. The magnitude of the second stage is little affected by the first-stage operation, since the only difference between the second stage and the one-stage resection is that the common duct is closed off rather than used as a choledochojejunostomy.

TECHNIC

The technic of pancreatoduodenal resection will not be presented in this paper, but the order of procedure will be briefly summarized.

The duodenum and pancreas are elevated by division of the peritoneum, carrying the dissection

under the superior mesenteric vessels. The two anterior layers of the gastrocolic omentum are then divided, freeing the distal third of the greater curvature of the stomach. The gastrohepatic ligament is next divided, with ligation of the right gastric artery. Following this, the common duct is elevated and the portal vein demonstrated to be free under the pancreas. To determine this, it may be necessary to ligate and divide the gastroduodenal artery at the upper border of the pancreas. If resection is then shown to be feasible, the prepyloric area of the stomach is divided between clamps. Careful dissection of the common duct must be done, and if a previous stage of cholecystjejunostomy has been performed, the common duct must be divided well below the entrance of the cystic duct. If there is any doubt of the patency of the cystic duct when the common duct is turned in, it must be reopened and implanted in the jejunum, leaving two biliary anastomoses. The pancreas is then elevated, with division at the neck if there is carcinoma of the ampulla and through the body if there is carcinoma of the head of the pancreas, followed by ligation of the duct of Wirsung. The junction of the third and fourth portions of the duodenum is severed in carcinoma of the ampulla, but in carcinoma of the head of the pancreas the jejunum is sectioned 5 cm. below the ligament of Treitz and the upper jejunum and fourth portion of the duodenum are withdrawn under the superior mesenteric vessels. The resection is completed by dissection of the uncinate process, and the entire block is removed in one piece.

The reconstruction is done in the following order. The pancreas is closed by mattress sutures, and a transfixion silk suture is passed through the duct of Wirsung proximal to the tie.[9] The pancreatojejunal anastomosis is then completed, utilizing the afferent loop of jejunum. In the one-stage procedure, anastomosis of the common duct is done 5 cm. distal to the pancreatojejunal anastomosis over a tube, following which an end-to-end gastrojejunostomy is carried out. If the latter is done to the efferent loop of jejunum, it is an end-to-side anastomosis and no enteroenterostomy is necessary, but if it is done proximally, it should be followed by the jejunojejunostomy.

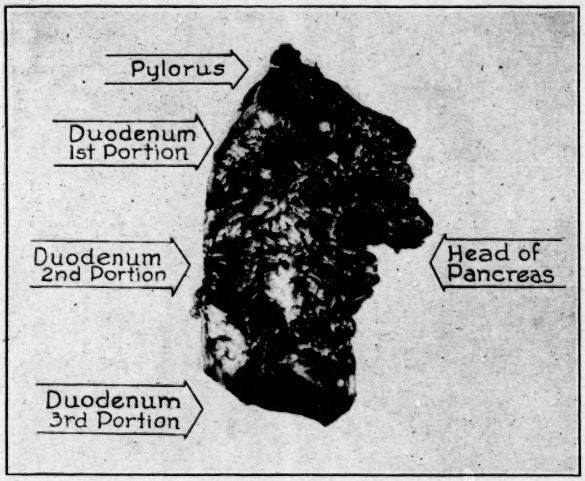

FIGURE 3. *The Serosal Surface of a Pancreatoduodenal Resection. The pyloric end of the stomach, the duodenum and the head and neck of the pancreas are visible.*

CLINICAL MATERIAL

Eighteen patients have been submitted to pancreatoduodenal resection. Ten additional patients had a first-stage operation, with a second operation planned. One refused the second procedure, 1 was considered to be in too poor condition to withstand it, in 1 case operation was discontinued because of vessels resembling hemangioma throughout the operative field, 2 patients were found to be inoperable because of metastases, 1 had involvement of the superior mesenteric vessels, and 1 had a benign tumor that could be locally removed from the

ampulla. In addition, 3 patients were explored at the second stage; after freeing of the pancreas no tumor was found, and the operation was discontinued.

The first patient was operated on in August, 1939, and the remainder have been operated on since August, 1942. During the two-year period from August, 1942, to August, 1944, 51 patients with carcinoma of the pancreatoduodenal region have been observed, with 24 having no operation or having exploration, drainage of the common duct or cholecystjejunostomy performed for palliation only.

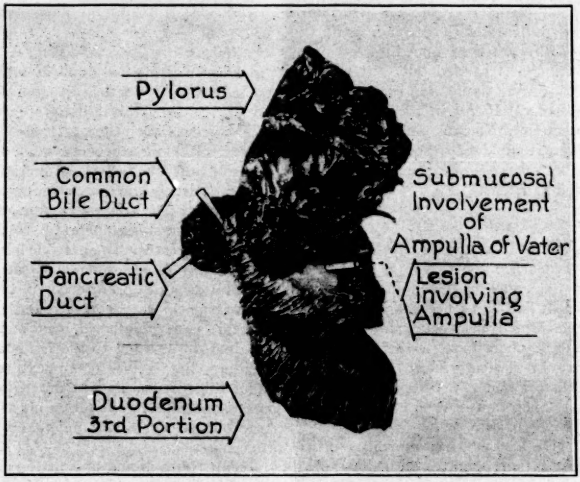

FIGURE 4. *The Mucosal Surface of a Pancreatoduodenal Resection. The circumscribed adenocarcinoma projects through the duodenal wall.*

Seventeen patients were submitted to radical resection during this period, and in an additional 10 the second stage was planned but not done.

Comprising these 18 cases in which operation was performed, there were 13 men and 5 women. Two patients were between forty and forty-nine years old, 8 between fifty and fifty-nine, 6 between sixty and sixty-nine, and 2 over seventy. One of the patients explored at the second stage with no tumor being found was only twenty-seven years of age; with the age incidence in this series cancer seems unlikely to occur at such an early age.

Four patients had had symptoms for less than one month, 6 for one to three months, 4 for three to six months, and 1 for six to twelve months. Three had had symptoms for over a year.

The presenting symptom in 16 cases was jaundice, and in 2 other patients anemia of unexplained origin was found. Weight loss was a conspicuous symptom, with only 2 patients having none. The average weight loss was 20 pounds, and 1 patient lost 42 pounds in six months. Anorexia, weakness, malaise, diarrhea, mushy stools, pruritus and indigestion were frequent later symptoms. One patient had severe epigastric pain, with deep jaundice, but at the time of operation was found to have gallstones and carcinoma of the ampulla.

The laboratory findings were similar to those of other abdominal cancers. The blood bilirubin was consistently elevated, varying from 1.6 to 21.4 mg. per 100 cc. The 2 patients without clinical jaundice had a bilirubin of 1.6 and 1.9 mg., respectively. The prothrombin time was little affected.

Preoperative Diagnosis

The diagnosis of stones in the common duct was made in 4 cases, cancer of the stomach in 1, retroperitoneal sarcoma in 1, in which there was no jaundice, and cirrhosis of the liver in 1. Six patients were operated on with a diagnosis of carcinoma of the pancreas, and a diagnosis of carcinoma of the ampulla was made in 8. Two diagnoses were made in 3 cases, so that twenty-one diagnoses are listed for the 18 cases. Common-duct stone and cancer of the pancreas were diagnosed in 1 case, carcinoma of the ampulla and cirrhosis of the liver in 1, and common-duct stone and carcinoma of the ampulla in 1.

Because of the painless jaundice in all but 1 of 15 cases, it is evident that the diagnosis of carcinoma of the pancreas, ampulla or biliary tract should have been made oftener.

Pathology

Thirteen of the 18 patients had carcinoma of the ampulla, although one of these was a carcinoid without metastasis; 3 had cancer of the pancreas; 1 had a large carcinoma of the second portion of the duodenum, and in 1 patient no cancer was found. This high preponderance of carcinoma of the ampulla in this series of 18 cases may give an incorrect idea of the incidence of malignancy in this area, since in many of the patients with carcinoma of the pancreas the process was too advanced for resection. In 1 case, resection was carried out, but without question some cancerous tissue was left. The fact that so few cases of carcinoma of the pancreas are suitable for resection makes us believe that the operation of pancreatoduodenal resection at present offers little hope for any case of extensive carcinoma of the head of the pancreas.

Operation

Five patients had a one-stage pancreatoduodenal resection, with 1 death. The two-stage operation, as described by me,[9] was employed in 13, with 2 deaths. One patient had had a first-stage cholecystduodenostomy performed elsewhere, and a second had had a two-stage operation elsewhere that was discontinued because of hemorrhage. These cases were of course listed under two-stage resections, although only one operation in each case was done by us.

The 3 deaths give an operative mortality of 17 per cent. The first patient operated on in 1939, died of hemorrhage. This occurred through an external pancreatic fistula and did not seem to be alarming in amount, but the patient succumbed two days later, on the seventeenth postoperative day. An autopsy did not reveal the site of bleeding, and no other cause for death could be determined; the death was listed as having been due to secondary hemorrhage. Because of reaction around the ligated stump of the gastroduodenal artery it was suspected that the hemorrhage had occurred from this source. The second death, in March, 1943, occurred from shock and anuria twenty-eight hours after operation. The third death, in May, 1943, occurred sixty-two days postoperatively. Autopsy showed pyelonephritis, with cortical abscesses, retroperitoneal sepsis and pericarditis.

Subsequent Results

These patients have been observed over too short a period of time to report late results. One patient has been well for two years, 5 for eighteen months, 4 for a year, and 3 are in good condition, having been operated on within the past year.

There have been 2 deaths subsequent to discharge from the hospital. The first of these patients had an extensive carcinoma of the duodenum with lymph-node metastases and died eight months postoperatively. The second had an extensive carcinoma of the pancreatic head, and at the time of operation it was thought that some cancerous tissue was left. Death followed in ten months from recurrence with generalized abdominal metastases.

Thirteen of the 18 patients are living and in good condition. One patient has had mild recurrent epigastric discomfort, and 2 have had transient attacks of chills and fever. None have had recurrent jaundice. All have maintained their nutrition.

Summary

Eighteen pancreatoduodenal resections are reported, with 3 deaths, an operative mortality of 17 per cent. Clinical data are presented briefly.

The general plan of operative management is discussed. The one-stage operation was employed in 5 cases, and the two-stage operation in 13. Since many patients are over sixty years of age, have severe obstructive jaundice and are in poor condition, the two-stage operation is considered necessary in most cases. An antecolic long-loop cholecystjejunostomy is recommended, since it permits rehabilitation and does not complicate the resection. Restoration of the external pancreatic juice to the intestine is accomplished by direct anastomosis of the duct of Wirsung to the jejunum as a means of avoiding the serious complication accompanying pancreatic fistula, and in order that normal pancreatic and digestive function may be accomplished. Antecolic gastric, biliary and pancreatic anastomoses are advised.

Results for a period up to two years are reported, with satisfactory results in 13 of 18 patients.

Present experiences demonstrate that pancreatoduodenal resection for carcinoma can be successfully carried out.

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THE CARDINAL MANIFESTATIONS OF PAROXYSMAL TACHYCARDIA*

II. Vascular Collapse

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VASCULAR collapse is frequently associated with paroxysmal tachycardia. The medical literature consists for the most part of single case reports and reveals that whereas in some cases collapse is associated with rapid ventricular rates, in others it is absent with equally rapid rates.[1–15] I[16] have observed vascular collapse in 15 of 125 cases of tachycardia, and have pointed out that it occurred only under specific conditions, thus justifying its designation as one of the cardinal manifestations of paroxysmal tachycardia. In the present study 128 new cases have been added to the 125 previously reported, making a total of 253. All cases had an electrocardiogram confirming the presence of an abnormal rhythm and providing the ventricular rate during the paroxysm. To evaluate the role of tachycardia in the genesis of vascular collapse, cases in which circulatory failure was apparent before the onset of paroxysmal tachycardia were excluded. This study accordingly concerns the 40 patients (16 per cent) in whom vascular collapse complicated paroxysmal tachycardia, and 21 in whom vascular collapse did not occur despite extremely rapid heart rates. This larger series has confirmed the previous conclusions and has furnished additional facts of clinical interest and importance.

Table 1. *Correlation Between Vascular Collapse and Ventricular Rate in Two Hundred and Fifty-Three Cases of Paroxysmal Tachycardia.*

Ventricular Rate	Cases with Collapse	Cases without Collapse	Total Cases
Less than 180	13 (6%)	192	205
180 or more	27 (56%)	21	48
Totals	40	213	253

Vascular Collapse

The ages in the 40 cases ranged from thirteen to eighty-eight years, with 4 cases in the fourth decade, 7 in the fifth, 9 in the sixth, 14 in the seventh and 4 in the eighth decade. Paroxysmal auricular tachycardia and paroxysmal auricular fibrillation were each present in 13 cases (33 per cent), and paroxysmal auricular flutter and paroxysmal ventricular tachycardia each in 7 cases (18 per cent). The ventricular rate ranged from 130 to 233, but was less than 180 in only 13 cases. The rate was 200 or more in 18 cases, 180 to 199 in 9, 170 to 179 in 5 and less than 150 in 4 cases. There were no signs of organic heart disease in 12 patients, 2 of whom had hyperthyroidism; the ventricular rate in these cases was 200 or more in 6, 180 to 189 in 3, 170 to 179 in 2 and 140 in 1. It is noteworthy in itself that 12 of the 40 patients had normal hearts, but even more revealing is the fact that the ventricular rates were not significantly slower in the 28 patients with organic heart disease than in those with structurally normal hearts. Vascular collapse and paroxysmal tachycardia were noted in 9 cases with acute or recent myocardial infarction, the collapse and tachycardia occurring later than the tenth day in 7 of them; the ventricular rate was 200 or more in 3, 180 in 2, 170 to 179 in 2 and 160 and 145, respectively, in 2 cases. In 7 cases of coronary heart disease, with a past or present history of angina pectoris or old myocardial infarction or post-mortem evidence of coronary-artery disease, the rate was 200 or more in 3, 190 in 1, 187 in 2 and 160 in 1. There were 6 cases of mitral stenosis (1 with coronary heart disease), and the ventricular rates were 200 or more in 4, 187 in 1 and 140 in 1. A case of subacute bacterial endocarditis and dissecting mycotic aneurysm of the aortic valve had the slowest ventricular rate in the entire series, namely, 130. There were 2 cases of aortic and mitral valvular disease with ventricular rates of 170 and 200, re-

Table 2. *Age Distribution of Cases with and without Collapse.*

Age by Decades	All Cases with Vascular Collapse	Cases with Collapse and Ventricular Rates of 180 or More	Cases without Collapse and Ventricular Rates of 180 or More
First	0	0	2
Second	1	1	0
Third	0	0	0
Fourth	4	3	3
Fifth	7	7	3
Sixth	9	6	7
Seventh	14	6	6
Eighth	4	3	0
Ninth	1	1	0
Totals	40	27	21

Table 3. *Distribution of Various Types of Tachycardia in Cases with and without Collapse.*

Rhythm	Cases with Vascular Collapse		Cases without Vascular Collapse*	
	No.	Per-centage	No.	Per-centage
Paroxysmal auricular fibrillation	13	33	7	33
Paroxysmal auricular flutter	7	18	1	5
Paroxysmal auricular tachycardia	13	33	10	48
Paroxysmal ventricular tachycardia	7	18	3	14

*Ventricular rate 180 or more.

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spectively. There was 1 case of cor pulmonale, with a ventricular rate of 187, 1 case of pericarditis with a rate of 214, 1 case of hypertensive heart disease with a rate of 150 and 1 case of heart enlargement of undetermined etiology with a rate of 166. Frank congestive failure was observed in only 6 cases, and the ventricular rates in these were 210, 200, 187, 170, 140 and 130, respectively. The slowest rates were noted in 7 cases complicated by pulmonary embolism — 140 in 2 cases and 150, 160, 166, 170 and 175, respectively, in 5. There were only 6 other cases in which the ventricular rate was less than 180. One of these patients had free aortic insufficiency, and another mitral and aortic stenosis. The third had chest pain and paroxysmal auricular fibrillation with a rate of 160 on the tenth day of acute myocardial infarction. Four hours after the onset of the arrhythmia and one and a half hours after the second intramuscular injection of quinidine, when the ventricular rate had dropped to 130, vascular collapse suddenly appeared and death occurred half an hour later. In another case, vascular collapse and paroxysmal ventricular tachycardia with a rate of 145 occurred on the thirteenth day after acute myocardial infarction. Quinidine restored normal rhythm, which was maintained until the patient's death fourteen days later; during this period the temperature and white-cell count were elevated and vascular collapse recurred several times. Paroxysmal auricular tachycardia with a ventricular rate of 170 induced vascular collapse in an eighty-year-old man; the heart was normal and there were no complicating factors; stimulation of the carotid sinus interrupted the tachycardia, with immediate resumption of a normal circulation. The last patient in this group had mild vascular collapse with paroxysmal auricular tachycardia and a ventricular rate of 177; his heart was normal, and although he was seventy years old, he had had similar attacks, according to his own statement, for twenty years.

TABLE 4. *Cases of Vascular Collapse with Ventricular Rates of Less than 180.*

Case No.	Age	Rhythm	Ventricular Rate	Diagnosis	Comment
	yr.		*per min.*		
9	53	Paroxysmal auricular fibrillation	160	Angina pectoris	Pulmonary embolism
12	64	Paroxysmal auricular fibrillation	170	Recent myocardial infarction	Pulmonary embolism
30	57	Paroxysmal auricular tachycardia	130	Subacute bacterial endocarditis; congestive failure.	Free aortic insufficiency
31	70	Paroxysmal auricular tachycardia	177	Normal heart	Mild collapse; attacks for 20 years.
124	34	Paroxysmal auricular fibrillation	140	Mitral stenosis; congestive failure.	Pulmonary embolism and infarction; autopsy.
133	64	Paroxysmal auricular fibrillation	170	Mitral stenosis; aortic stenosis; congestive failure.	Aortic stenosis
145	64	Paroxysmal ventricular tachycardia	175	Recent myocardial infarction	Large pulmonary infarct
149	62	Paroxysmal ventricular tachycardia	145	Acute myocardial infarction	Recurrences of collapse later during normal rhythm
153	65	Paroxysmal auricular fibrillation	150	Hypertensive heart disease	Phlebitis; pulmonary embolism and infarction.
179	60	Paroxysmal auricular tachycardia	166	Large heart (questionable etiology)	Pulmonary embolism; shock continued after normal rhythm restored.
180	66	Paroxysmal auricular fibrillation	140	Normal heart	Phlebitis and pulmonary embolism
197	80	Paroxysmal auricular tachycardia	170	Normal heart	
235	62	Paroxysmal auricular fibrillation	160	Acute myocardial infarction	Shock appeared 4 hours after the onset of paroxysmal auricular fibrillation and chest pain; there was possible fresh myocardial infarct or possible pulmonary embolism with a probable toxic quinidine reaction.

Extremely Rapid Rates Without Vascular Collapse

Vascular collapse is not invariably induced when extremely rapid ventricular rates are attained. Forty-eight patients in this series had rates of 180 or more, but without vascular collapse in 21. The 2 youngest patients were two and six years old, respectively, and there were 3 patients each in the fourth and fifth decades, 7 in the sixth and 6 in the seventh decade. Seven patients (33 per cent) had paroxysmal auricular fibrillation, 10 (48 per cent) paroxysmal auricular tachycardia, 1 (5 per cent) paroxysmal auricular flutter and 3 (14 per cent) paroxysmal ventricular tachycardia. The ventricular rate was 200 or more in 11 cases, — the fastest rate being 250 in a two-year-old child, — 180 to

189 in 8 and 190 to 199 in 2. The rate in 8 patients with normal hearts, including 2 cases of hyperthyroidism, was 200 or more in 6, 193 in 1 and 180 in 1. Paroxysmal tachycardia did not induce vascular collapse in 2 cases of acute myocardial infarction, 1 of which was further complicated by congestive failure; the ventricular rates were 188 and 187, respectively. The rates in 5 other cases of coronary heart disease — 1 of them with complicating hyperthyroidism — were 215, 190, 188, 187 and 180, respectively. In 3 cases of hypertensive heart disease the rate was 200, 200 and 180, respectively, and in a case of subacute bacterial endocarditis it was 200. Two patients with cardiac enlargement of undetermined etiology had ventricular rates of 187 and 214. Frank congestive failure was noted in 4 cases, and the rates were 215, 200, 200 and 187.

TABLE 5. *Data on Ten Cases of Congestive Heart Failure, Six with Vascular Collapse and Four without Vascular Collapse despite Ventricular Rates of 180 or More.*

Case No.	Age	Rhythm	Ventricular Rate	Diagnosis	Comment
	yr.		per min.		
30	57	Paroxysmal auricular tachycardia	130	Subacute bacterial endocarditis; free aortic insufficiency.	Vascular collapse
46	41	Paroxysmal auricular fibrillation	210	Mitral stenosis	Vascular collapse
115	65	Paroxysmal auricular flutter	187	Mitral stenosis; coronary heart disease.	Vascular collapse; autopsy.
124	34	Paroxysmal auricular fibrillation	140	Mitral stenosis	Vascular collapse; pulmonary embolism and infarction; autopsy.
133	64	Paroxysmal auricular fibrillation	170	Mitral stenosis; aortic stenosis.	Vascular collapse
227	75	Paroxysmal ventricular tachycardia	200	Acute myocardial infarction	Vascular collapse
16	63	Paroxysmal auricular tachycardia	200	Pneumonia; diabetes.	No vascular collapse
18	54	Paroxysmal auricular tachycardia	215	Hypertensive and coronary heart disease	No vascular collapse; autopsy.
49	60	Paroxysmal auricular tachycardia	200	Hypertensiye heart disease	No vascular collapse
127	44	Paroxysmal ventricular tachycardia	187	Recent myocardial infarction	No vascular collapse; autopsy.

Discussion

When vascular collapse is associated with paroxysmal tachycardia, the one factor invariably present is an extremely rapid ventricular rate. The critical rate level for the induction of collapse is in the vicinity of 200, which is consistent with the observations of Wiggers[17] that the total cardiac output falls when the heart rate exceeds 180. That this is the only necessary factor is evident from the fact that collapse is induced by extreme rates in cases with normal hearts uncomplicated by severe infection, embolism, surgery and so forth. The importance of the rate is shown by 2 cases of paroxysmal auricular tachycardia with auricular rates of 233 and 214, respectively, and intermittent 2:1 auriculoventricular block; signs of circulatory failure were evident at the faster ventricular rates, but promptly disappeared when the ventricular rates halved. Similarly, vascular collapse was not induced by paroxysmal auricular tachycardia at a rate of 150 in a patient with a normal heart, but promptly appeared a few days later with the onset of a second paroxysm at a rate of 186. The duration of the paroxysm and the type of cardiac mechanism do not appear in themselves to be decisive in provoking circulatory failure. The lesser incidence of paroxysmal auricular fibrillation and the correspondingly greater incidence of the other types of tachycardia in the cases with collapse than in the entire series are due to the fact that extremely rapid ventricular rates are less frequent in paroxysmal auricular fibrillation than with other mechanisms.[16] Congestive failure plays no part in the genesis of vascular collapse. The age factor is largely unimportant, except that circulatory failure may be induced by somewhat slower rates in the aged than in younger patients. With aortic valvular disease, collapse may be induced at rates considerably below the critical level.

Vascular collapse occurred in 27 of 48 cases with ventricular rates of 180 or more, but in only 13 of 205 cases in which the ventricular rate was less than 180; the view that an extremely rapid ventricular rate, and it alone, is responsible for circulatory failure is strengthened by a review of these 13 cases. One of the patients had mild collapse with a ventricular rate of 177, which is too near the critical rate level to require any comment; an eighty-year-old man had collapse with a rate of 170, and 2 patients had aortic valvular disease. Pulmonary embolism, in addition to paroxysmal tachycardia, was present in 7 cases and, as is well known, may itself be respon-

sible for vascular collapse. The data in the 2 remaining cases, presented above in detail in the section on vascular collapse, clearly indicate that factors other than tachycardia were present and at least partly responsible for the circulatory failure; the late appearance of collapse, with sudden death shortly after its onset in one of them, and recurrence of collapse after restoration of normal rhythm in the other, are not to be expected when collapse is due solely to extreme tachycardia; an untoward quinidine reaction may have been present in one of the cases.

TABLE 6. *Analysis of the Forty-Eight Cases with Rates of 180 or More according to the Diagnosis and to Whether Vascular Collapse Occurred.*

DIAGNOSIS	CASES WITH RATE OF 180–199	CASES WITH RATE OF 200 OR MORE	ALL CASES
Normal heart:			
Collapse	3	6	9
No collapse	2	6	8
Acute or recent myocardial infarction:			
Collapse	2	3	5
No collapse	2	0	2
Coronary heart disease:			
Collapse	3	3	6
No collapse	4	1	5
Mitral stenosis:			
Collapse	1	4	5
No collapse	0	0	0
Hypertensive heart disease:			
Collapse	0	0	0
No collapse	1	2	3
Other types of heart disease:			
Collapse	1	1	2
No collapse	1	2	3
Totals	20	28	48

The question why extremely rapid rates induce collapse in some cases but not in others cannot be answered from the above data; even soon after recovery from vascular collapse unassociated with paroxysmal tachycardia, extremely rapid rates may fail to induce circulatory failure. It is interesting that, in the absence of complicating factors, the critical level for the ventricular rate is not lower in cases of myocardial infarction or other types of heart disease—with the exception of aortic valvular disease — than it is in normal hearts. Nevertheless, when the critical rate level is reached or surpassed, the susceptibility to collapse is somewhat different in the various groups. Vascular collapse is induced by rates of 180 or more in about half the cases with normal hearts and of those with coronary heart disease, in about three quarters of the cases of acute or recent myocardial infarction and in all the cases of mitral stenosis. Collapse did not occur in the 3 cases of uncomplicated hypertensive heart disease, a number too small to warrant any conclusions.

When vascular collapse is induced by paroxysmal tachycardia, it promptly disappears when the abnormal rhythm is abolished or a significant reduction of the heart rate is effected. When this does not happen, some factor other than the tachycardia must have caused the collapse. Other factors must be sought also when collapse occurs with rates well under 200, except in cases of aortic valvular disease. The most frequent additional factor in this series was pulmonary embolism.

SUMMARY

The clinical data of 253 cases of paroxysmal tachycardia are analyzed with reference to the occurrence of vascular collapse.

Vascular collapse occurs under constant conditions and is therefore one of the cardinal manifestations of paroxysmal tachycardia; it occurs in 16 per cent of the cases.

Extreme tachycardia itself induces vascular collapse in more than half the cases with rates at or above the critical level, which is in the vicinity of 200; below this level, collapse is not induced by tachycardia alone. The critical level is not lower in cases of myocardial infarction or other types of heart disease, with the exception of aortic valvular disease, than in normal hearts.

Extremely rapid ventricular rates induce vascular collapse in about half the cases with normal hearts and with coronary heart disease, in about three quarters of the cases of acute or recent myocardial infarction and in all the cases of mitral stenosis.

Causes other than tachycardia must be suspected when collapse is associated with rates well under 200 or when termination of the abnormal rhythm or significant reduction of heart rate is not promptly followed by resumption of a normal circulation.

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MEDICAL PROGRESS

SCARLET FEVER (Concluded)*

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EPIDEMIOLOGY

There has been a marked decline in the severity of scarlet fever in the last thirty years.[40] The mortality rate has dropped materially in the northern states, but this has not been apparent in the South.[41] Furthermore, as pointed out by Stebbins,[41] where the incidence of scarlet fever has declined there is not always a comparable reduction in the incidence of other streptococcic infections. This statement applies more to states and municipalities than to military organizations.

In the last few years the newer technics of identifying beta-hemolytic streptococci have been used in several studies of the epidemiology of scarlet fever. These studies give a rational explanation of how this disease is spread from person to person and how epidemics start and spread, and point out the factors that appear to be necessary in the control of this disease. The work of Keefer and his associates[38] on the epidemiology of scarlet fever has already been described. Schwentker, Janney and Gordon[4] made a study of streptococcal infection in Rumania over a period of three years, and have pointed out many of the important factors having to do with the epidemiology of the diseases produced by this group of organisms. They found that there is a gross mathematical relation between the incidence of scarlet fever in a country and its latitude. In temperate countries, the logarithm of the morbidity was found to be directly proportional to the latitude, whereas in the tropics streptococcal diseases are rare. In this connection, they neglect to bring out that whereas these diseases are not prevalent at sea level in the tropics, they become extremely prevalent at high altitudes, as in Bogotá and Mexico City.

These authors noted that no one of several serologic types of streptococcus was universally responsible for the disease over the world, although in any given country one or a few types usually predominated. The incidence of any one type among the total scarlatinal strains varied from time to time, one type gradually diminishing as another increased in frequency. It was found that more than one group or type of streptococcus could be recovered from the throats of healthy carriers as well as those of convalescent carriers, but that patients with acute disease usually harbored only one serologic type. In Rumania there was a cyclic rhythm in the gross and Group A carrier rates, the highest rate occurring during the late autumn and winter, and the lowest in the summer months. The same incidence with respect to season applies to New England, and this carrier rate is directly correlated with the incidence of streptococcal infections, which are also most frequent in the fall and winter and least prevalent during the summer months. In a study of the carrier problem in Rumania, Schwentker and his co-workers found that the gross and Group-A carrier rates bore a crude direct relation to each other, whereas the carrier rates for all groups other than Group A remained constant. They concluded that the incidence of scarlet fever is dependent on the carrier rate rather than the reverse.

In a study of the different serologic types present in the various villages in which the work was done, it was shown that all the known types of streptococci could be found but that the majority occurred only infrequently. In each village a few types predominated in general, but the outstanding bacterial flora was different for each community. Many of the types fluctuated in frequency of occurrence with time. The streptococcal types most frequently found in scarlet fever also caused most of the other streptococcal diseases in the same region. The same types that produced disease were also the ones that were prevalent in carriers. The differences in streptococcal flora between communities with and without scarlet fever were slight, and greater than between two different areas free from scarlet fever. From these facts it was concluded that some condition other than lack of scarlatinal strains must have been responsible for the absence of scarlet fever. A study was also made of the Dick reaction. It was found that in villages free of scarlet fever the distribution of positive Dick reactions in various age groups was the same as in other parts of the world, as has been described above. The percentage distribution of positive Dick reactions had much the same general pattern as the age distribution of cases of scarlet fever.

An epidemic of scarlet fever due to a Type 10 strain of hemolytic streptococcus was studied. Just before the outbreak of the epidemic there occurred an increase in the gross, Group A and Type 10 carrier rates, and this increase was maintained until almost the end of the epidemic. Patients who developed tonsillitis without a rash were shown to be infected with the same type of streptococcus.

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All those who came down with scarlet fever were shown to be Dick positive. Among those who escaped infection some were Dick positive and others Dick negative; these did not become ill in spite of the fact that they were proved by culture to be harboring the causative agent. It was concluded that they must have had a sufficient degree of antibacterial immunity to protect them.

These authors give a concise and clear description of their conception of the epidemiology of scarlet fever:

> A scarlatinal strain of streptococcus, either newly introduced or already present in a community, is distributed throughout the population. The number of persons reached depends on the distribution factor, as previously described [measured by the carrier rate]. The distribution factor determines the degree of dissemination of the streptococcus in the community, and by the law of chance, the greater the dissemination, the greater the number of persons who will come in contact with the organism. Some persons escape contact with the streptococcus entirely; these naturally remain well. Among the others who are reached by the organism, some will be resistant by virtue of antibacterial immunity. Regardless of their Dick reaction or antitoxic immunity, they remain well. These persons either eliminate the organism promptly or become healthy carriers. Those without antibacterial immunity sicken. The Dick-positive individuals, having no antitoxic immunity, develop scarlet fever; those with antitoxic immunity have streptococcal tonsillitis without the scarlatinal rash. The difference is purely clinical. Should the portal of entry be other than the nasopharynx, the relationship is still the same. Puerperal fever may develop with or without the scarlatinal rash; or erysipelas or some other kind of infection may occur. From the three groups of individuals who harbor the streptococcus, the organisms are still further distributed and the cycle repeats itself.

Schwentker, Hodes, Kingsland, Chenoweth and Peck[42] studied a company of sailors in "boot training" in whom there occurred an outbreak of streptococcal infection. Six different types of streptococci were found to be responsible for sickness in the company. Of these, Types 1 and 6 were outstanding. Together they accounted for 30 of 42 cases of infection. These types did not cause scarlet fever. The 2 cases of scarlet fever that occurred were both due to Type 3. The percentage distribution of the various types was the same among cases of illness as in normal carriers. The distribution of the various types among normal carriers in six other companies on the station was practically the same as in the study company. In all companies, Types 1 and 6 predominated. Nevertheless, among cases of scarlet fever occurring at the station, Types 3 and 19 were outstanding. No case of scarlet fever due to Type 6 was discovered, and only 2 were due to Type 1. It appeared that the streptococci present at the station could be divided into two types — those that were highly pathogenic but had little scarlatigenic ability, and those that were scarlatigenic as well as pathogenic.

The carrier rate of streptococci was found to be high in the groups that were studied. Whereas the rate in the general population is usually 10 per cent, at this station it was found to be as high as 69 per cent. Where more than one type of streptococcus was active during an outbreak, the number of cases due to each type was found to be proportional to the carrier rate for the respective type. This makes it appear that the carrier was instrumental in transmitting the disease. The high carrier rates were found to develop among the men during the period of training, because only 4 per cent of incoming inductees were found to harbor beta-hemolytic streptococci.

A group of 73 men who did not develop any illness were also studied. These men remained well in spite of the fact that as many as five different types of streptococci of known pathogenicity were recovered from their throats. The Dick reaction apparently played no role in resistance to infection, since the amount of illness in Dick-negative men was proportionately the same as that in Dick-positive ones. Some persons were found to resist infection with one type of streptococcus but became ill when infected with another type. No person was found who had two illnesses due to the same serologic type of streptococcus. It is interesting that the authors were able to show that some of the strains isolated from those who had a streptococcal infection without a rash — that is, no scarlet fever — were capable of producing erythrogenic toxin.

Schwentker[42] also studied the role of the carrier in the spread of an epidemic of streptococcal infection. He observed an epidemic of scarlet fever in an Army camp due to an organism that gave reactions with both Types 17 and 23 by the Griffith technic and with Type 19 by the Lancefield precipitin method. These findings were due to the fact that the organism contained T antigens of both Types 17 and 23 but M antigen only of Type 19. The number of cases of scarlet fever in different companies studied varied from zero to 10 per cent. The case incidence was found to be related to the carrier rate for the Type 19 strain of streptococcus causing the outbreak. The logarithm of the incidence of scarlet fever was directly proportional to the Type 19 streptococcus carrier rate. The same relation was found to exist between the incidence rate of the disease and the gross (all groups) and Group A carrier rate, but in each of these cases it was merely a reflection of the Type 19 relation. The carrier rates for groups other than Group A and for all Group A strains except for Type 19 were found to be roughly the same in all companies.

In 1944, Coburn[44] reported some studies on the problem of the role of the carrier in the transmission of streptococcal disease. He described two outbreaks set up by carriers. In a group of 200 patients with throat infections due to Type 19 streptococcus,

some of whom had scarlet fever whereas others did not, there were two persons who proved to be dangerous carriers after discharge from the hospital, both giving rise to additional cases. One of these men had an acute pharyngitis followed by mastoiditis, sinusitis and bronchitis. He gave rise to 4 cases of scarlet fever or acute pharyngitis during readmission to the hospital for a mastoidectomy. The other man had a sinusitis and a focal pneumonitis following an attack of scarlet fever and later, while in an orthopedic ward containing 40 bed patients for observation following a minor head injury, was responsible for 16 cases of streptococcal infection in that ward. In neither carrier was the number of streptococci in the throat culture found to be large, and in neither of them was the organism highly invasive. In both, however, the communicability was high and outbreaks occurred. Coburn believes that a high degree of communicability, and thus a dangerous carrier state, may be acquired by the streptococcus during secondary infections and during an outbreak of virus infections of the respiratory tract. The latter finding is in direct contrast to that of Schwentker, Janney and Gordon, who were unable to demonstrate any effect of the incidence of the common cold or the nonspecific infection referred to as "influenza" on the incidence of streptococcal infection.

Communicability in the two patients described by Coburn was thought to cease when the infectious process subsided under the influence of sulfonamides. In discussing the property of communicability, Coburn expresses the belief that this is acquired by an adaptive change in the bacteria with relation to the changing immune state in the host under conditions of an infection in which neither the host nor the bacterium can promptly establish supremacy. Because of the change, the bacteria become able to multiply in the presence of inhibitory substances present in the normal mucous membranes and thus become host-fast. This property may be quickly lost, but so long as it exists the organisms have a high degree of communicability. Coburn speculates that fundamentally this phenomenon may depend on the development of adaptive enzyme systems.

A study of the factors concerned in the transmission of streptococcal infections has been made by Hamburger.[45] It was found that when only as few as one or two carriers were present, cross-infection spread rapidly on open wards where there were patients with streptococcal infections. On the other hand, cross-infection might not occur if as high as 50 per cent of the patients on a ward were harboring Group A streptococci in their throats. Subclinical cross-infections by hemolytic streptococci were found to be not infrequent. Patients who were recovering from German measles seemed to share the well-recognized susceptibility of patients with measles to streptococcal infection. These authors also point out that there is insufficient proof that because a person is a streptococcal carrier he is responsible for cases of infection, since he may be harboring a serologic type entirely distinct from that producing disease.

Hamburger[46] also made a study of the content of the saliva of 156 patients who had beta-hemolytic streptococci in their throats, studying this as a factor in the transmission of streptococcal infections. He found that in the acute stages of scarlet fever over 80 per cent of the patients had the same serologic type of beta-hemolytic streptococci in the saliva as in the throat. In the remainder of the patients no streptococci were demonstrated in the saliva. Several day-to-day patterns of streptococcal content of the saliva were found to exist. In 51 per cent of the patients, the number of hemolytic streptococci in the saliva diminished with the passage of time, usually gradually but in some cases abruptly. In 25 per cent, there was no change in the salivary flora during a period of weeks; about half these showed the presence of streptococci in the saliva, and the other half showed none. Hamburger could find no significant difference in the number of hemolytic streptococci in the saliva at various stages of the scarlet fever as compared with that from cases of tonsillitis and pharyngitis without a rash. In patients who had had their tonsils removed it was found that hemolytic streptococci were present in smaller numbers and for shorter periods than in those in whom the tonsils were still present.

Hamburger and his associates[14] also made a study of the air and the floor dust in a ward and the bedclothes in their relation to the transmission of streptococcal infections. They found that air-borne organisms were present in large numbers in wards in which streptococcal disease was present, and that these were most numerous around the beds of patients whose respiratory secretions contained the largest numbers of streptococci. They showed that the number of organisms in the air is important in any consideration of the role that air plays in transmission of disease, and that even a small number of streptococci in the air are capable of producing disease in a susceptible person. Thus, a technician who was working on a streptococcal ward became infected when the number of organisms present in the air was shown to be less than 1300. It is pointed out that the reservoir from which the organisms get into the air is the floor dust and the bedclothes of patients with streptococcal infections. Therefore, the control of air-borne streptococcal infection in hospital wards may be largely a question of control of the secondary reservoirs in dust and bed linen. Hodes and his co-workers[47] have studied scarlet fever as an air-borne infection. They conclude that the direct transmission by air from a patient with scarlet fever is a more important means of spread

than is the general reservoir of air. Wheeler and Jones[48] have demonstrated that one of the most significant factors in the genesis of epidemics is the rapid introduction of susceptible persons into an infected population, as in the reception of recruits.

From these more recent studies on the epidemiology of scarlet fever several pertinent facts become obvious. First, epidemics of this disease are usually due to one or two serologic types of streptococcus, whereas sporadic cases may be due to any of the types that have been described. Furthermore, just preceding and during an epidemic there is often an increase in the carrier rate of the serologic types that are most prevalent in the sick. The exact role of the healthy carrier in the transmission of streptococcal infections is not clear. The studies of Foley, Wheeler and Aycock[49] indicate that the spread of scarlet fever through secondary cases is not limited to case-to-case transfer, but includes nonscarlet-fever and subclinical infection as well as intermediate carriers. Schwentker, Janney and Gordon[4] and some of the other workers who have been cited maintain that the so-called "healthy carrier" may be an important factor in the dissemination of streptococci, with the subsequent production of actual infection. Coburn's[46] hypothesis regarding the adaptive abilities of the streptococci with respect to their degree of communicability deserves further investigation. Hamburger's[14] investigations have emphasized the well-known significance of the role played by air, floor dust and bedclothes in the transmission of streptococcal infections in hospital wards. The crowding together of large numbers of men from various parts of the country in the various establishments of the armed forces has afforded an exceptional opportunity for studying the epidemiology of outbreaks of streptococcal disease in sufficiently large numbers to yield invaluable data, in drawing conclusions from which the greatest care must be taken. There is still much to be learned concerning the epidemiology of the streptococcal infections.

Methods of Control

Granting that scarlet fever is merely one manifestation of streptococcal infection and is dependent on the ability of the invading strain to elaborate an erythrogenic toxin in a susceptible host, it becomes clear that many persons may harbor toxin-producing strains without manifesting signs of scarlet fever. First, the person may be a carrier and thus show no manifestation of disease. It has been seen that the carrier rate of the epidemic strain often rises abruptly prior to and during an epidemic, but this fact does not establish that cases of scarlet fever originate from carriers. The recent studies of Hamburger[45] in an Army hospital cast some doubt on the part played by the healthy carrier in the spread of scarlet fever. Thus, although the carrier index may give valuable warning concerning a probable outbreak of an epidemic of scarlet fever and the etiologic type, the carrier is not necessarily the means of spreading the disease, unless he himself succumbs to an invasion of the streptococcus and becomes ill. Further studies are necessary to determine whether as a result of the illness he may change from a harmless carrier to a dangerous one. The complexity of this problem from the standpoint of extremely mild or so-called "missed" cases is apparent.

The carrier here referred to is not to be confused with the patient who is convalescent from scarlet fever and still harbors the etiologic strain in some localized infection, whether this be a subacute rhinitis, tonsillitis, otitis media, paronychia or discharging wound. Aside from such a low-grade infection he may be afebrile and enjoy good health, but such a person is not a healthy carrier in the true sense of the term.

After uncomplicated scarlet fever the upper respiratory tract usually returns to normal by the end of the second week in adults and by the end of the third week in children. It is often difficult to say just what constitutes normality, since only parts of the upper respiratory tract are visible on examination. Therefore, some patients may seem to be clear of infection at the end of the isolation period and yet be capable of infecting others. If this were the only source of scarlet fever, one might consider the advisability of a longer period of isolation, but prolonged isolation has not reduced the incidence of scarlet fever. A small percentage of the uncomplicated cases are still infectious after four weeks. When scarlet fever is epidemic, there are always many persons about with sore throats but without the rash who disseminate the same streptococci as freely as those with the full-blown rash — indeed, much more so, since they are apt to be out and about rather than confined to bed. This is the explanation of the inability to control scarlet fever adequately by isolation in the home or in the hospital. If all patients with streptococcal disease were isolated instead of only those with one manifestation of streptococcal disease, something approaching control might be accomplished. But here again one is confronted by the fact that streptococcal infections, as determined by the presence of antistreptolysin, may be so exceedingly mild as to go unnoticed.[4,40] The role played by such subclinical cases in the spread of these infections is unknown. Certainly any attempt to control scarlet fever by quarantining carriers is impractical. Likewise it is difficult to control the influx of susceptible persons into an infected population. This has, however, been done with success in controlling an epidemic.[47] Thus, stopping the reception of raw recruits stops the spread of the disease as definitely as when new patients are refused admission to a ward where scarlet fever has broken out. Without new fuel a fire dies out.

In certain streptococcal epidemics an extremely high proportion of the cases exhibit scarlet fever. In others the opposite is true. In either instance it is inconsistent to isolate those with a rash for four weeks and to isolate the others for only the duration of the fever or not at all.

The new conception of scarlet fever has brought about a reduction of the isolation period in many cities in the United States. Three weeks for children and two weeks for those over seventeen years of age are now recommended by the Massachusetts State Department of Health. This is a gesture in the right direction, but it is still arbitrary. In Bergen and Trondheim in Norway, prior to the German invasion, scarlet fever was left to the attending physician to handle as a streptococcal infection, the rash being disregarded.[18] After eighteen years the results were sufficiently satisfactory to justify continuing the abolition of any set period of isolation. Aberdeen in Scotland followed this example and was still satisfied with the ruling after five years of a similar experiment.

Hospitalization

Hospitalization for streptococcal disease, including scarlet fever, should depend on circumstances. Isolation at home is desirable if the case is mild or moderate and exhibits no serious complications. The patient with a mild case who is placed on an open scarlet-fever ward is more liable to have a relapse and to have complications than if he were left at home. Poverty or unco-operative parents may be proper indications for hospitalization. Hospitalization is desirable in all severe cases and in all threatening complications, such as mastoiditis, sinus empyema and nephritis. Stockholm furnishes an excellent example. There, according to the latest accounts,[61] hospitalization for scarlet fever is required by law. Every case goes to the hospital, not because hospitalization has reduced the incidence of scarlet fever, but because the mortality rate has been found to be lower in the hospital in spite of open ward care than in the home. In other words, hospitalization affords better results through the prompt and effective handling of complications. If all patients with severe cases and complications were promptly hospitalized, the same good results would be obtained. Every possible effort should be made to avoid the overcrowding of scarlet-fever wards. The policy in this regard at the Belmont Hospital in Worcester deserves the greatest praise.

The hospital, then, should serve for those cases arising in homes where facilities for good care do not exist. It stands to reason that hospitalization is necessary for those mild cases that arise in military establishments and in boarding schools, colleges and other institutions where people are herded together in dormitories. Thus it is that in a large educational center, such as Greater Boston, adequate facilities for the hospitalization of upper respiratory streptococcal disease should be available; furthermore, such hospitalization to be effective as a means of control should not be confined to those manifesting the rash of scarlet fever. It is particularly desirable that patients should be sent to a hospital when other members of the household are food handlers. Thus, hospitalization does play its part in the control of the disease. It should by no means be a routine procedure but should be applicable only to the exigencies of the individual situation.

Inconsistencies in Regulations

Not long ago a nurse after attending a case of scarlet fever was required to take a week off before signing on again for general nursing, in spite of the fact that she took a bath and changed her clothes on coming off the contagious case, whereas the doctors who insisted on this outrageous ruling had so little conception of contagious technic that they often went directly to other patients without even washing their hands. Other doctors donned caps, gowns and masks, insisted on having sheets soaked in bichloride of mercury hung in the doorway, and after examining the patient put their hands in their pockets to get their watch, glasses, handkerchief or thermometer. They then relied on dipping their hands in an antiseptic solution rather than washing them in soap and water. It is well to remind the medical profession of these sins of the past. Or shall it be admitted that the contagious technic of too many eminent physicians is vastly inferior to the aseptic technic of all eminent surgeons?

A child is sent to the hospital with scarlet fever, and at the same time another child in the family has a sore throat. The second child is not allowed at school but plays with her schoolmates on the street and goes to motion-picture shows. Any attempt to curtail the second child's activities is objected to by the parents on the ground that the child with the scarlet-fever case has been isolated in the hospital and that the other child has only a sore throat. Education of the public is sorely needed, but what chances are there of impressing the public when there is no agreement on isolation periods? The State Department of Public Health merely makes recommendations regarding isolation, whereas the local boards of health make the rules. Hence it is that in Greater Boston there is a wide variation in the requirements. A patient over seventeen years of age with uncomplicated scarlet fever is isolated for two weeks in Boston and Newton, for three weeks in Cambridge and Brookline and for four weeks in Lexington. If he lives in Boston he can go back to work in Lexington for the last two weeks of his convalescence, because Lexington has no report of his having had scarlet fever. The ignoring of the advice of the Department of Public Health by some local authorities leads to confusion and to lack of confidence in the methods of control.

In a certain military establishment the practice is to hospitalize all patients with upper respiratory streptococcal disease under the diagnosis of streptococcosis, and to isolate those with uncomplicated cases of scarlet fever. At the end of not over fourteen days these patients are allowed to leave by the main gate and to mingle with the townspeople. But these same military authorities insist that a carpenter employed in the erection of a new building in this establishment shall be laid off work for four weeks without pay because his young son has scarlet fever at home. It is, indeed, extremely difficult to educate the public to co-operate with the medical profession in the control of streptococcal disease when the laity sees the perpetration of such glaring inconsistencies.

Chemoprophylaxis

The control of streptococcal infections and their sequelae, including rheumatic fever, through mass prophylaxis with small doses of sulfonamides has been carried out extensively in the last two years.[47, 55–57] The morbidity rate has been a serious problem in certain localities where these organisms flourish. Several recent reports in the literature indicate a successful program of control. Sulfonamide-resistant strains, however, are beginning to show up to a disturbing extent in certain localities.

Watson and his co-workers[55] reported their results in a study of the use of sulfadiazine in a Navy establishment in 1943. They were faced by an epidemic of scarlet fever due to a Group A, Type 19, beta-hemolytic streptococcus. As soon as the epidemic began all the personnel at the station were given 0.5 gm. of sulfadiazine twice a day. During the first week after the start of the sulfonamide therapy, the incidence of scarlet fever dropped markedly. In another group of men who did not receive daily dosage of the sulfonamide the incidence of scarlet fever remained high. When this second group was given the same dosage of sulfadiazine, there was a similar reduction in new cases. After the sulfonamide was discontinued scarlet fever remained absent. The carrier rate for Type 19 still remained high, although there was some reduction. The average blood level for the drug in the men who were treated was 2.5 mg. per 100 cc. Of the several thousand men treated prophylactically only 3 developed toxic manifestations in the form of a rash. No severe toxic reactions were observed.

A study of the same problem in the Army Air Forces by Holbrook[58] showed that when acute rheumatic fever became prevalent it was always preceded by a high incidence of hemolytic streptococcus infections. A 50 to 75 per cent reduction in the incidence of respiratory diseases and streptococcal infections was accomplished by the use of sulfadiazine prophylaxis under carefully controlled conditions in a significantly large troop population. A study of the data indicated that a reduction in the incidence of rheumatic fever paralleled the reduction in the occurrence of respiratory and streptococcal diseases.

Coburn[56] has reported his observations on the use of sulfadiazine prophylaxis against streptococcal infection in a group of 30,000 men stationed at three different Navy camps. It was found that the ingestion of 1 gm. of the drug daily accomplished the following things: outbreaks of streptococcal infection were checked at their onset, well-advanced outbreaks of streptococcal disease appeared to be checked in their spread, and 85 per cent of the susceptible recruits were protected from implantation with bacterial respiratory pathogens. It seemed that a continuous daily dosage of 0.5 gm. of sulfadiazine yielding an average blood concentration of 1.4 mg. per 100 cc. and one of 0.8 mg. per 100 cc. in the respiratory secretions was almost 85 per cent effective in preventing implantation of *Str. haemolyticus*. The only untoward effects noted in this experiment in mass sulfadiazine prophylaxis were the occurrence of evanescent rashes in 0.5 per cent of the patients treated and severe constitutional reactions in 0.01 per cent.

The largest group of subjects in whom the experiment of mass prophylaxis with sulfadiazine has been attempted is mentioned in a recent report by the Bureau of Medicine and Surgery of the Navy Department,[58] covering observations carried out for a period of six months, with 600,000 men receiving daily doses of the drug. It was found that sulfadiazine, in either prophylactic or therapeutic doses had little effect on the throat flora of carriers of hemolytic streptococci. Implantation of streptococci was prevented regardless of the pathogenicity of the strains that were prevalent, although in some instances the organisms were able to overcome the inhibitory effects of sulfadiazine. This occurred after the drug in doses of 1 gm. daily had been ingested for several weeks, and was observed in areas where exposure to streptococcal infection was greatest and at times when the incidence of measles was high. Usually, however, it was evident that the presence of sulfadiazine in the secretions of the nasopharynx prevented the implantation of a new strain of hemolytic streptococcus and prevented frank infection in 95 per cent of the persons given the drug.

The percentages of untoward reactions observed were the same as those previously noted by Coburn[56] in the study of chemoprophylaxis in a smaller group of naval personnel. It is pointed out that coincident virus infections, particularly measles and influenza, increased the communicability of hemolytic streptococci, but that prophylaxis with sulfadiazine was highly effective in preventing the implantation of the bacteria in the upper respiratory tract of susceptible groups of persons living in camps in which measles was present. No sulfonamide-resistant strains were encountered, and there was no evidence

of such resistance during the six months that the study was carried out. There is some suggestion, however, that in the final month Type 19 may have developed some degree of fastness to the sulfadiazine, since at that time this organism became the prevalent one at several establishments. The importance of this problem to the Navy is stressed by the following quotation:

> In these groups of naval personnel a saving of a day per man per month can be expected when bacterial respiratory pathogens are active. If the center's recruit complement is 30,000 and all hands receive sulfadiazine prophylaxis, one can anticipate a saving of 30,000 hospital days each month during seasons conducive to respiratory diseases. This is equivalent to freeing a 1000-bed hospital and all the labor and personnel associated with the care of the sick.

Keith and his associates[57] found that sulfadiazine in 1 gm. daily doses reduced hospital admissions for nasopharyngitis and scarlet fever to one third in a station of the Canadian Navy. Hodges[54] found this drug equally effective in this respect among troops in the United States Army.

The data that have been presented on the effect of prophylaxis with small doses of sulfadiazine for the prevention of outbreaks of scarlet fever and for the control of epidemics already under way are indeed impressive. The effect that this program has had in the saving of man-hours of duty in the armed forces has certainly been extremely helpful to the war effort.

Although mass prophylaxis with sulfonamides has been used extensively and with striking success in the armed forces, it must be kept in mind that this was carried out under medical supervision. This, of course, could be done under equally good medical supervision in boarding schools and similar institutions, but it is questionable whether it should be recommended for the population at large. Furthermore, tabulated reports from the stations where sulfonamide-resistant strains prevail have not been published, and we have yet to be told whether such mass prophylaxis encourages the development of sulfonamide-resistant strains.

* * *

The recognition that scarlet fever is not a disease entity is a milestone of progress, but there is still much to be learned about the pathogenesis of scarlet fever and its complications, its mode of spread and the possible role of carriers. Active immunization is a valuable means of protection, but this is indicated only where the chances of exposure are great, as in nurses' training schools. Great care should be taken in the selection of those to be immunized, as well as in the method employed. Serum therapy and chemotherapy have proved to be effective weapons in prophylaxis and treatment, but both these measures have distinct indications and definite limitations.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

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CASE 31191

PRESENTATION OF CASE

A sixty-nine-year-old gateman was admitted to the hospital because of jaundice, nausea and vomiting.

Three weeks before admission he noticed that his abdomen had become quite distended, and six days before entry he developed nausea and vomiting, which persisted until admission. He also observed that the urine was "dark." During the week before admission he passed only an occasional small scybalous stool, despite taking three Alophen pills each day. Usually two pills resulted in three movements a day. Three days before admission his physician noticed that he was icteric. He had experienced no pain, weight loss, anorexia or weakness. He became quite short of breath on climbing a long flight of stairs and had occasional cramp-like pains in the calves and feet. He had recently noticed difficulty in starting to urinate. Until the present illness he had always been active and well.

His wife and five children were in good health.

Physical examination revealed a mildly icteric man, with a moderately severe right scoliosis. He had varicose veins, as well as telangiectatic vessels over the legs and feet. The breath sounds were diminished over the right chest posteriorly. The heart was normal, and the pulse strong. The liver edge was felt well below the level of the umbilicus, even to the left of the midline. The left lobe of the liver was enlarged, as indicated by percussion over the posterior chest wall, and the spleen was not felt; the abdomen was otherwise negative. A large fairly smooth prostate was palpated.

The temperature, pulse and respirations were normal. The blood pressure was 165 systolic, 90 diastolic.

Examination of the blood showed a red-cell count of 5,600,000 and a white-cell count of 12,400, with 82 per cent neutrophils. The stool was formed, dark and guaiac negative. The urine was acid, with a specific gravity of 1.020, and gave a + test for albumin, a ++++ test for bile and a green precipitate with Benedict's solution; it contained 30 white cells per high-power field and showed a positive urobilinogen test in a dilution of 1:512. The serum nonprotein nitrogen was 125 mg. per 100 cc., the cholesterol 192 mg. and the phosphorus 4.2 mg. The total protein was 5.78 gm. per 100 cc., with an albumin-globulin ratio of 1.8. The van den Bergh test was 10.6 mg. direct and 13.6 mg. indirect, the cephalin flocculation test ++++, the alkaline phosphatase 11.5 Bodansky units per 100 cc., and the prothrombin time 19 seconds (normal, 18 to 20 seconds).

An electrocardiogram showed a normal tracing. X-ray examination revealed a marked right dorsal scoliosis. The right diaphragm was somewhat elevated. Several linear areas of increased density were seen in the right lower lung field. The aorta was tortuous and calcified in the arch. The heart was not remarkable. By fluoroscopy the liver appeared enlarged.

On the third hospital day the patient became progressively more stuporous, responding only to pain. The temperature rose to 100.5°F. The pulse and respirations became moderately elevated. He became comatose and expired quietly on the fourth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. MARIAN W. ROPES: It is apparent that this patient had severe liver-cell damage, and I believe that his death was due to hepatic failure.

The disease, in so far as he was aware of it, was of short duration, a total of three and a half weeks, and there was some evidence in the laboratory studies to indicate that the acute liver damage was also of rather short duration. For instance, in severe liver-cell damage a prothrombin time of 19 seconds — a perfectly normal reading — is unusual if such damage has persisted for a long period of time. Similarly, in liver failure of considerable duration a normal cholesterol level is a somewhat unusual finding, a low reading usually being expected. If there is an obstructive element, an elevation on this basis might balance the lowering due to parenchymatous damage. I am sure, however, that this differential is not reliable. Furthermore, in liver damage of long duration one expects more of a decrease in the serum albumin and an elevation of the globulin. The other tests give adequate evidence of liver-cell damage — the high urobilinogen, the ++++ cephalin flocculation test, the high van den Bergh values and the high nonprotein nitrogen. I assume that the increase in nonprotein nitrogen was due to an increase in amino acids, — the usual finding in cases of hepatic failure, — and I suspect that the urea was only slightly elevated. There is little or no evidence of renal failure. The phosphatase level is somewhat higher than one would ordinarily expect in parenchymatous liver damage of short duration and suggests a slight element of obstruction, as does, theoretically, the high direct-indirect ratio in the van den Bergh test. Obviously

*On leave of absence.

if any obstruction was present, it was relatively minimal compared to the parenchymatous damage.

One must next consider what caused this damage. Probably the most significant factor is the large size of the liver. May we look at the x-ray films?

DR. MILFORD D. SCHULZ: You can see this great mass filling the entire epigastrium. If it is not liver, it cannot be distinguished from it. The diaphragm is somewhat elevated. What this airless area in the right lung field is, I cannot say.

DR. ROPES: Assuming that the mass is liver, there surely is no question that it is tremendous.

DR. SCHULZ: I agree.

DR. ROPES: The first problem to be considered is whether an acute liver disease, such as acute infectious hepatitis, can produce this picture. Against that is the size of the liver, it being extremely unusual to observe a liver of this size at any stage of acute hepatitis, particularly at a terminal stage, when acute failure and death are imminent. Similarly, I should expect the spleen to be palpable in a hepatitis of this degree.

There are two other acute liver diseases that should be mentioned in passing. Thus, acute liver poisoning from any source might be considered on the basis of the history, but the large liver and the lack of further details permit us to discard this cause. Similarly there is no evidence for an infectious process, such as Weil's disease. So the evidence, to me, indicates underlying liver disease in which there was final failure of the remaining liver cells due to some superimposed factor.

There are three possibilities to consider: syphilis, a malignant tumor and cirrhosis. Unfortunately we are not told anything about the Hinton and Wassermann tests. The size of the liver, particularly that of the left lobe, demonstrated by a test that Dr. Aub will perhaps mention later, namely, posterior chest percussion, is entirely consistent with syphilis. Although syphilis cannot be ruled out, it also cannot be proved in this case.

A malignant neoplasm, either primary or secondary, must be considered. If it were metastatic carcinoma, it would be unusual to have so few symptoms, including absence of weight loss, up to three and a half weeks before death. Also there is no evidence of a primary source. Constipation came on during the last few weeks of life, and I interpret this as being secondary to hepatic failure rather than indicating a lesion of the gastrointestinal tract. I do not believe that the patient had prostatic carcinoma. If a malignant tumor was the etiologic factor, the course is more consistent with a primary carcinoma of the liver than with a metastatic lesion.

The third possibility is portal cirrhosis. There is no evidence of the biliary type from either the history or the laboratory findings. It is possible, although unlikely, for portal cirrhosis to cause a liver of this size, with left lobe enlargement. The absence of symptoms up to the terminal event, with failure of the residual liver cells, is not inconsistent. I think again, however, that the relatively slight change in some of the chemical findings would be unusual in a cirrhosis of this duration and degree. Also, I should have expected more in the way of anemia, splenic enlargement and further evidence of portal-vein obstruction.

In addition there were arteriosclerosis, prostatic hypertrophy and something in the right lower chest that may have been atelectasis secondary to the liver enlargement. I doubt that this was related to the primary process in any other way.

To summarize, I think that this man died because of hepatic failure and that he had underlying liver disease before the final terminal damage of the remaining liver cells. I favor a malignant tumor, although it is absolutely impossible to rule out syphilis.

DR. BENJAMIN CASTLEMAN: Do you want to go any farther in classifying the tumor?

DR. ROPES: I believe that it was a liver-cell carcinoma.

DR. JOSEPH C. AUB: I thought that this man had a primary tumor in the liver on the basis of hepatoma. I have always believed that these usually occurred in the left lobe of the liver, although Dr. Castleman disagrees with me.

Dr. Ropes has asked me to demonstrate one way of pointing out the size of the left lobe of the liver. One should percuss down just to the left of the spine until one comes to flatness; having come to flatness, one should percuss out laterally to resonance. This is a sharp line that should be 5 cm. from the midline in a normal person. With a big left lobe of the liver, it may measure 8 or 9 cm. The reason for this is that, the left lobe of the liver being in the back just behind the stomach, resonance develops when the liver edge ends and the gas bubble in the cardiac end of the stomach begins. This gives a quite accurate indication of left-lobe enlargement.

DR. CASTLEMAN: In our experience hepatomas are more frequent in the right lobe than in the left; when the left lobe is enlarged, we think oftener of syphilis than of primary tumor.

DR. CHESTER M. JONES: I am interested in the emphasis that Dr. Ropes has put on syphilis, since I would not have seriously thought of it. The liver was very large by the x-ray films and on physical examination, indicating a diffuse process, which I suppose would be called a cirrhosis. In a syphilitic process I believe that the physical findings are different — the mass is lobular.

In this case I thought immediately of primary hepatoma. Furthermore, primary hepatoma, or even metastatic cancer of the liver, may go for a long period of time without producing many symptoms or much interference with liver function, except when superimposed on cirrhosis. There is a difference in statistical figures, if one compares what we see here with what they see on the West Coast.

Wilbur, Wood and Willett* report primary hepatoma without cirrhosis in a high percentage of cases; our cases are usually superimposed on cirrhosis.

DR. CASTLEMAN: About 90 per cent of our cases are associated with cirrhosis.

DR. JONES: There is an end picture of hepatic failure, as this patient exhibited, in any form of diffuse liver disease. In the final stage it is essentially the same clinical picture, regardless of whether the failure is due to acute yellow atrophy, infection, a specific toxin or any other cause. Incidentally, I should think that one would have found an enlarged spleen if this were a syphilitic cirrhosis, just as in any other form of cirrhosis.

DR. CASTLEMAN: For a syphilitic liver to be as big as this one was it would have to be the hepar lobatum type, which as a rule does not lead to liver failure unless acute hepatitis of some sort is superimposed. Acquired diffuse syphilitic cirrhosis is extremely rare, and I doubt that the liver would be so large.

CLINICAL DIAGNOSIS

Liver-cell carcinoma.

DR. ROPES'S DIAGNOSES

Liver-cell carcinoma.
Arteriosclerosis.
Pulmonary atelectasis: right lower lobe.
Prostatic hypertrophy.

ANATOMICAL DIAGNOSES

Malignant lymphoma, lymphoblastic type, involving liver, mesenteric and retroperitoneal lymph nodes and vertebral bone marrow.
Arteriosclerosis.
Pulmonary fibrosis and emphysema: right lower lobe.
Prostatic hyperplasia.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: At autopsy the liver weighed 5000 gm., a tremendous liver. We do not usually see livers of that size, and when we do, they are almost always due to metastatic carcinoma. We have one liver of this size due to so-called "Hanot's cirrhosis," that is, a biliary type of cirrhosis. I believe that we had one or two almost that size during the extreme fatty stage of acute alcoholic hepatitis before the onset of fibrosis.

The liver was infiltrated with grayish-white, obviously neoplastic tissue, and we assumed that it was metastatic carcinoma. The mesenteric and retroperitoneal nodes were also involved, but we were unable to find the primary site. Microscopic examination showed why we did not find it. The tumor proved to belong to the malignant-lymphoma group. Most of the liver cells were completely replaced by cells of the lymphocytic series, predominantly lymphoblasts. There was no cirrhosis. Except for the mesenteric and retroperitoneal lymph nodes, which were replaced by neoplasm, the only other organ involved was the vertebral bone marrow.

The prostate was enlarged and showed hyperplasia. The abnormal x-ray shadow in the chest proved to have been due to fibrosis of the lungs with large emphysematous blebs in the right lower lobe.

*Wilbur, D. L., Wood, D. A., and Willett, F. M. Primary carcinoma of liver. *Ann. Int. Med.* 20:453-485, 1944.

CASE 31192

PRESENTATION OF CASE

A fifty-three-year-old engineer was admitted to the hospital because of mental confusion and severe headache of approximately twenty hours' duration.

Five years before entry he passed an examination for life insurance. The patient had been well and active until one year before admission, when he began having severe headaches at night, and was found to have a systolic blood pressure of 225 and albuminuria. Despite severe headaches he continued to work. At noon on the day before admission the patient had some teeth extracted. The oral surgeon reported that the patient did not look well and appeared somewhat confused. Two hours later the patient telephoned his wife and complained of pain in the jaw. Three hours later he called her again and told her that he was extremely sick. In the meantime his automobile was found in a badly wrecked condition. When the patient was found, it was observed that he had a small bruise on his forehead. He had no recollection of an accident, but he did recall wandering about the city, in the early afternoon, constantly bumping into people and being unable to find his office. At home that evening he spoke incoherently and appeared to be blind. During the night he complained of headache and was able to get up and go to the bathroom twice. On the following morning he was brought to the hospital.

Physical examination revealed a well-developed, poorly nourished, pale, sweating, extremely drowsy man who complained of a throbbing frontal headache. There was a small bruise on the forehead. The alveolar sockets were bleeding. All but the canine teeth had recently been extracted. The heart border was 8.5 cm. to the left of the midsternum in the fifth interspace. The sounds were distant and of poor quality. There were frequent extrasystoles. A systolic murmur was best heard at the apex. The dorsalis pedis arteries were easily felt. There was diminished visual acuity, with a left homonymous hemianopsia. Fundoscopy showed choked disks, retinal hemorrhages and spasm of the arteries, with marked bilateral arteriovenous nicking. There was a left lower facial weakness, but no weakness of arm or leg was detected. The

neck was moderately stiff. There was a bilateral Kernig's sign. The left knee jerk was more prominent than the right. The abdominal reflexes were absent on the left. There was a questionable extensor plantar reflex on the left side.

The rectal temperature was 100°F., the pulse 105, and the respirations 10. The blood pressure was 220 systolic, 120 diastolic.

The urine was slightly alkaline, with a specific gravity of 1.014, and gave a ++++ test for albumin; the sediment showed 10 to 15 white cells, 8 to 10 red cells and 3 granular casts per high-power field. Examination of the blood revealed a red-cell count of 4,200,000 and a white-cell count of 20,600, with 88 per cent neutrophils. The stool appeared normal and was guaiac negative. The serum nonprotein nitrogen was 40 mg. per 100 cc., the protein 8 gm., and the carbon dioxide 29 milliequiv. per liter. A lumbar puncture gave an initial pressure equivalent to 300 mm. of water. All three tubes appeared equally "bloody," and the fluid contained 5850 red cells and 3 lymphocytes per cubic millimeter, but no polymorphonuclears; the supernatant fluid was xanthochromic. A spinal-fluid Wassermann test was negative, and the total protein was 129 mg. per 100 cc. The patient's headache was improved following the lumbar puncture. A lumbar puncture on the second day revealed an initial pressure equivalent to 350 mm. of water; there were 7800 red cells, 1400 polymorphonuclears and 700 lymphocytes per cubic millimeter, but no organisms were seen on smear. Cultures of the spinal fluid, urine and blood showed no growth.

An x-ray examination of the skull was negative. The pineal gland was calcified and not displaced. A chest film showed the heart to be prominent in the region of the left ventricle. The aorta was tortuous. There was evidence of healed pulmonary tuberculosis.

An electroencephalogram was grossly abnormal; the high-voltage, slow activity that constituted this abnormality appeared to be strongest in the anterior half of the head and was symmetrical except in the occiput where it was more marked on the left than on the right.

On the second day the patient was drowsier and more disoriented. No petechiae were seen. The temperature and pulse remained unchanged, and the respirations were about 20. The blood pressure varied from 220 systolic, 120 diastolic, to 240 systolic, 140 diastolic. The heart border was found by several examiners to lie 12 cm. from the midsternum in the fifth interspace. The pulmonic second sound was slightly greater than the aortic. The lungs were clear. The edge of the liver was felt two fingerbreadths below the costal margin. There was no edema or dyspnea. The neurologic examination showed no change except for absent abdominal and cremasteric reflexes and increased rigidity of the neck. There was right horizontal nystagmus. The extraocular muscles were normal, and the pupils reacted normally to light. The ophthalmoscopic findings were unchanged.

On the third hospital day the patient suddenly began to gasp, became unconscious and cyanotic and, within a few minutes, expired.

Differential Diagnosis

Dr. Madelaine R. Brown: This is a remarkable case history and if I miss the diagnosis, it certainly will be my own fault. When I first read this record, it seemed to me to indicate a straightforward case of cerebral hemorrhage. After reading it a second time I began to see a few other things and it did not seem quite so simple.

We should consider several diagnoses. There are two that I need only mention. Brain tumor, such as angioma, may cause bleeding into the cerebrospinal fluid, but the onset here was sudden and the x-ray films showed that the pineal gland was in the midline; I think it unlikely that there was a tumor. The second diagnosis that needs mention is cerebral laceration. The patient bumped his head, but he had no fracture of the skull and I doubt that the blood was coming from a cerebral laceration. The conditions that we have to consider more seriously are a subarachnoid hemorrhage due to a ruptured aneurysm, a subdural hematoma and a cerebrovascular accident — either embolus, thrombosis or hemorrhage.

If we go back and attempt to reconstruct the story, the stage was set for a cerebrovascular accident. He had had hypertension for at least a year and possibly longer. He probably had cerebral arteriosclerosis and arteriosclerotic kidneys, and we know that he had retinal arteriosclerosis. He went to the dentist and had several teeth removed. Following this operation the dentist noticed that the patient was confused. Before the onset of a cerebral hemorrhage it is common for patients to complain of mental confusion, dizziness and headache. This patient knew that something was wrong and complained to his wife over the telephone that his jaw ached. He got into his car and started to drive, presumably to the office. He had an accident, probably because he lost consciousness. At least he remembered nothing about it, and the car was rather badly damaged. He escaped without any visible signs except a small bruise on the forehead. He got out of the car and started to wander around the city, although I do not know why he was allowed to. Apparently he bumped into people all the way because of his hemianopsia and could not find his office. Since he was able to walk, he had no hemiplegia, but he was confused and had a terrific headache. He again called his wife and said that he felt extremely ill. When he arrived home he was drowsy and confused but was well enough to get up and go to the bathroom that night. He still had no weakness

of the left side, but his headache became worse; he became more confused and finally was brought to the hospital. The next morning he had a stiff neck, bilateral Kernig signs, evidence of mental confusion and a spinal fluid that contained a great deal of blood.

If we try to localize this lesion before we discuss the nature of it, the electroencephalogram is not helpful. We have to depend on the clinical findings, and since all the signs are on the left, we must assume that the lesion was on the right side. What part of the right side? The hemianopsia seems to have been the most marked sign. Without hemiplegia or hemianesthesia we have to place the lesion in the occipital lobe, which indicates hemorrhage from the posterior cerebral artery and is rare. The most frequent source of cerebral hemorrhage is, of course, one of the short branches of the middle cerebral artery; the next is one of the long branches of the middle cerebral, then the anterior cerebral, the posterior cerebral and, finally, the basilar artery.

If we choose the posterior cerebral artery, even if it is an unusual site of hemorrhage, there are other signs for which we have to account — the weakness of the face, the questionable extensor plantar response, the hyperactive reflexes and absent abdominal reflexes on the left. So it seems to me that we have to make a diagnosis of two lesions: the second might have involved a small branch of the middle cerebral artery, supplying the right anterior central gyrus, or was possibly something outside the brain, such as a subdural hematoma.

If we place the chief lesion in the occipital lobe, what was its nature? Could there have been a subdural hematoma or ruptured aneurysm in the occipital area? Could there have been embolism or thrombosis rather than hemorrhage? It is possible that he had a subdural hematoma. He had an accident, and we know that people with arteriosclerosis are more susceptible to subdural hematoma than are those with normal vessels. But apparently the bruise on the forehead was a minor one. With a contrecoup effect one would expect involvement of the occipital region of the brain. It is possible, but not likely, that a recent subdural hematoma caused the blood in the spinal fluid, but it would not have caused the increased white-cell count, which usually comes from a rupture into the ventricle.

So far as aneurysm is concerned, certainly the homonymous hemianopsia is not typical of a ruptured aneurysm. Aneurysms of the cerebral vessels usually occur around the circle of Willis or at the beginning of the middle cerebral artery. It is possible that the mild hemiplegia was due to a ruptured aneurysm, but not the homonymous hemianopsia. So I do not believe that a ruptured aneurysm is likely.

Last of all we must consider the various kinds of vascular accidents. The chief lesion must have been a hemorrhage to account for the blood and white corpuscles in the spinal fluid. There may have been a secondary lesion in the low parietal area to account for the weakness of the face, and that might have been an embolus in a small branch of the middle cerebral artery, following extraction of the teeth — an infected embolus. Or it might have been another small hemorrhage, but that is difficult to say.

I shall close with the following diagnoses: generalized arteriosclerosis, particularly retinal, cerebral and renal; hypertensive heart disease; hemorrhage into the right occipital lobe, with rupture into the ventricle; and possibly an embolus in a small branch of the right middle cerebral artery.

DR. JOST MICHELSEN: How do you account for the retinal hemorrhages?

DR. BROWN: Simply by the increased intracranial pressure, which was equivalent to 300 mm. of water. He may have had a subdural hematoma in addition to account for such an increase in pressure, but it does occur only with hemorrhage.

DR. FRANCIS M. RACKEMANN: Is not the story of the slow development of symptoms against severe hemorrhage?

DR. BROWN: Patients with severe cerebral hemorrhage generally do not have a sudden exitus. They usually last about as long as this patient did — from twenty-four hours to three days.

CLINICAL DIAGNOSIS

Cerebral hemorrhage.

DR. BROWN'S DIAGNOSES

Cerebral hemorrhage, right occipital region, with rupture into ventricle.
Embolus, branch of right middle cerebral artery?
Generalized arteriosclerosis.

ANATOMICAL DIAGNOSES

Cerebral hemorrhage, right posterior parietal region.
Dissecting aneurysm of aorta, with rupture into pericardium.
Cardiac hypertrophy, hypertensive type.
Generalized arteriosclerosis.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: Before I call on Dr. Kubik to tell what was found in the brain I shall describe what was found in the heart.

This man was a hypertensive. He had a large heart, which weighed 500 gm. In the aorta just above the aortic valve was an intimal tear that had produced a dissecting aneurysm in the aorta as far as the arch, where it stopped (Fig. 1). This is quite unusual, for it is customary for a dissecting aneurysm to continue down the aorta into the abdominal portion and into the iliac vessels. This one stopped at the orifice of the right innominate artery, below which there was another intimal tear communicating with the aneurysm. There was an external rup-

ture through the adventitia at about the level of the proximal tear, so that there was a hemopericardium, which was the cause of the sudden exitus. This unusual condition could not have been suspected clinically.

DR. CHARLES S. KUBIK: There was moderate to marked arteriosclerosis, affecting particularly the basilar artery. There were small cerebellar and right temporal pressure cones. The right cerebral hemisphere was considerably enlarged because of a massive hemorrhage, 6 cm. in diameter, in the right posterior parietal region. There was no rupture into the lateral ventricle, but the ependyma of the inferior horn was blood stained, indicating that there had been some leakage, which unquestionably accounted for the bloody spinal fluid. Although cerebral hemorrhage may occur in practically any part of the brain, including the cerebellum, it is unusual in the posterior parietal or occipital regions. The most frequent site is the region of the lenticular nucleus, and the next, the pons, whereas a small number are scattered about in different places.

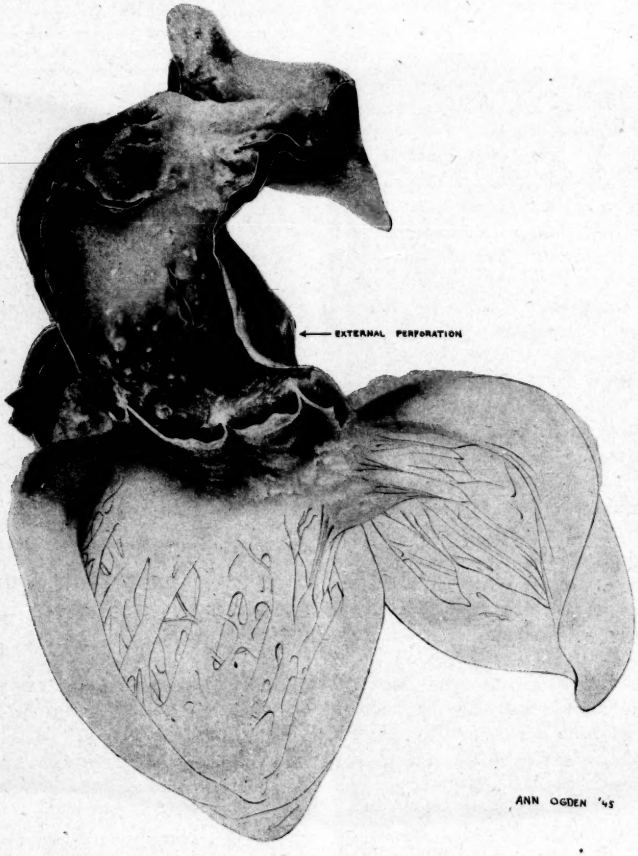

FIGURE 1.

DR. CASTLEMAN: It is interesting to speculate whether the accident had anything to do with the

dissecting aneurysm. We know that occasionally a dissecting aneurysm results from trauma. If this were so, there should have been evidence of trauma to the chest, which was lacking. The aorta did show medial degeneration or what is called "media necrosis cystica," which predisposes the aorta to the development of a dissecting aneurysm. I suppose that the symptoms that he might have had because of the aneurysm were masked by those of the cerebral hemorrhage.

DR. KUBIK: How old was the dissecting aneurysm?

DR. CASTLEMAN: Just a matter of a few days. The blood in the dissecting aneurysm was rather fresh, not the organized clot that one usually sees in an old dissecting aneurysm.

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PSYCHOSOMATICS

When, in 1822, William Beaumont, a native of Lebanon, Connecticut, exercised his Yankee ingenuity by holding a pannikin under Saint Martin's gastric fistula and catching the drippings, he was selling the world no wooden nutmeg. He was anticipating the work that Pavlov would do later with considerable refinement in technic, — Pavlov, for instance, early abandoned the use of gunfire in producing his fistulas, — and he was paving the way for the conclusions that Cannon would arrive at somewhat later on the bodily changes in pain, hunger, fear and the various subsidiary emotions.

Beaumont, in other words, laid the groundwork for a scientific approach to the study of mind and matter, and the influence of the former over the latter — a reality empirically accepted and never for an instant doubted by Bishop Berkeley, the homeopaths, the mesmerists, Elisha Perkins and the followers of Mary Baker Eddy.

Except for a few ardent and credulous cults, however, and a numerically less imposing group of psychologically and scientifically minded physicians, it has required for the population at large a second world war and a popular pictorial magazine to acquaint them with the actuality of psychosomatics.

It is time for the public to tire of chasing vitamins, as a cat chases its tail, having it always with him but never catching up with it — the matter of vitamins was practically settled, as we are beginning to learn, with the discovery of food. But the psychic origin of peptic ulcer is something new over which to agonize, and the thought that a cold in the head, an attack of asthma or a cardiovascular crisis may have its inception in the imagination is, for many, a novel idea with which to toy.

We had not, as a matter of fact, entirely failed to realize that an appreciation of the power of the intellect over our more earthy functions is no new idea, regardless of the enthusiasm of the neopsychosomatists. John Hunter proclaimed his life to be in the hands of any man who dared annoy him; followers of the cult of voodoo will lay themselves down and die if they so much as think that the witch doctors are after them; and a combat soldier in any war has known that no intestinal pathogen is necessary to produce an attack of uncontrollable diarrhea. Any radio listener, indeed, who has been unable to avoid suffering at the sound of a warbled commercial plug while waiting for his favorite commentator knows how these silly symphonies of the air may inspire in some of their hearers feelings of the blackest melancholy and, in others, those of incipient nausea.

It is something to be aware of the psychic stimuli that can erupt at the somatic level; when we can control them we may indeed know the peace that passeth understanding.

SCARLET FEVER AND STREPTOCOCCAL SORE THROAT

Some time ago the *Journal* called attention to the fact that the rules of isolation and quarantine now in force in many communities have not kept pace with present-day understanding of the epidemiology of certain infectious diseases.[1] This is particularly true with regard to scarlet fever, which has been singled out from the group of hemolytic streptococcus infections as the only one in which isolation and quarantine are required. Although patients with scarlet fever are quarantined for three or four weeks, there are no restrictions placed on cases of tonsillitis or pharyngitis, which may be equally important in spreading streptococcal infections, including scarlet fever.

An important step has recently been taken by the Department of Health of New York City in an attempt to remedy this situation. The provisions regarding scarlet fever have been changed in the latest revision of the Sanitary Code in that city to read as follows[2]:

1. The reportable disease scarlet fever is now included in a wider classification, namely, streptococcal sore throat, including scarlet fever.
2. The isolation period for streptococcal sore throat, including scarlet fever, is as follows:
   Uncomplicated case. Until the mucous membrane of nose and throat appear normal, but for not less than seven days after onset of the disease.
   Complicated case (discharging nose and ears, mastoids, enlarged or suppurating glands, pneumonia). Until recovery from the complicating condition, except that, if the complication persists for forty-five days from onset, two cultures not less than twenty-four hours apart may be taken, and if these are negative for *Streptococcus haemolyticus*, the case may be discharged. Such cultures must be submitted to and examined by the laboratory of the Department of Health.
3. Contacts are not excluded from school or work.
4. Visits by nurses to the homes of cases of scarlet fever are no longer required.
5. Children recovered from streptococcal sore throat, including scarlet fever, may be readmitted to school on a card issued by the Department of Health or the Department of Hospitals, or on a signed statement of a physician certifying that the child has recovered.

There will probably be some objections to the wording of the new regulations. It also remains to be seen whether they can be carried out as readily and effectively as the older ones. Nevertheless, it appears to be a step in the right direction. The efficacy of the older regulations in reducing the spread of infection has been seriously questioned, and it will be interesting to see whether these changes will in any way affect the epidemiologic pattern of scarlet fever and hemolytic streptococcus infections in New York City.

References

1. Editorial. Streptococcus sore throats and scarlet fever. *New Eng. J. Med.* 229:599, 1943.
2. Recent changes regarding scarlet fever. *Quart. Bull., Dept. of Health City of New York* 13:1, 1945.

MASSACHUSETTS MEDICAL SOCIETY

DEATH

MOIR — Marguerite W. Moir, M.D., of Boston, died December 3, 1944. She was in her seventy-second year.

Dr. Moir received her degree from Boston University School of Medicine in 1918.

MISCELLANY

PRIZE ESSAY

Modern Hospital has recently announced a competition for an essay on the subject "A Plan for Improving Hospital Treatment of Psychiatric Patients." Three prizes, totaling $900, will be awarded by the judges, who will be drawn from the United States Public Health Service, the American Psychiatric Association and the National Committee for Mental Hygiene. The competition is open to anyone except the judges and the employees of *Modern Hospital*, and all essays must be received by October 1, 1945. Further details may be obtained from the Modern Hospital Publishing Company, 919 North Michigan Avenue, Chicago 11.

NOTICES

ANNOUNCEMENTS

Dr. John B. Hall announces the removal of his office from 60 Windsor Street to 108 Dudley Street, Roxbury.

Dr. Savvas E. Theodore announces the removal of his office from 14 Chestnut Street, Springfield, to 510 Commonwealth Avenue, Boston.

MEDICAL ART SHOW

Modern Medicine's Medical Art Show will open at Yale University School of Medicine in the Harvey Cushing Room on May 20 and will continue until June 3. Previous showings at Baltimore's Enoch Pratt Library, the Cleveland Health Museum, the Minneapolis Public Library, Rochester's Rundel Memorial Building and the Brooklyn Public Library have attracted over 100,000 people. The work of the late Max Broedel, often called the father of medical art, together with that of many of the artists who studied with him in the School of Art as Applied to Medicine, which he founded at Johns Hopkins University School of Medicine, forms a large part of the exhibit. Included among the exhibitors is Miss Muriel McLatchie, head of the school of illustration at the Massachusetts General Hospital. The collection has been assembled by *Modern Medicine* as a tribute to the American medical artist, too long unknown and unsung, and yet such a vital factor in recording all progress in medicine.

(*Notices continued on page xvii*)